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CORRECTED VERSION

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

078996 A1

(54) Title: MEANS AND METHODS FOR MONITORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS

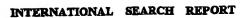
(57) Abstract: This invention relates to antiviral drug susceptibility and resistance tests to be used in identifying effective drug regimens for the treatment of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), particularly treatment regimens including a protease inhibitor. The invention further relates to the means and methods of monitoring the clinical progression of HIV infection and its response to antiretroviral therapy using phenotypic or genotypic susceptibility assays.



INTERNATIONAL SEARCH REPORT

International application No. PCT/US09/17178

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) :C12Q 1/18, 1/70, 1/68; C12N 15/85, 15/49						
US CL :435/5, 6, 32, 320.1; 536/23.72						
	national Patent Classification (IPC) or to both	national classification and IPC				
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols)						
		o by classification synaxols)				
U.S. : 424/9.2	2, 201.1, 208.1, 93.2; 435/5, @ .1, 320.1					
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched						
	·					
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)						
Please See Extra Sheet.						
C. DOCUMENTS CONSIDERED TO BE RELEVANT						
Category* Ci	tation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.			
'Ger ZDV	abase AIDSLINE, AN 1998:1910 notypic and phenotypic analysis //3TC/amprenavir combination the 12. Abstract No. 32312, page 58	1-12				
A US 5	5,766,842A (MELNICK et al) 16	13-24, 71-79				
HIV	ROBERTS, N. A. Drug-resistance patterns of saquinavir and other HIV proteinase inhibitors. AIDS. 1995, Vol 9, Suppl 2, pages S27-S32, see whole document.		25-33, 45-47, 54- 70			
frequence and	Database AIDSLINE, AN 1998:20452. HILL, A. et al. 'Low frequency of genotypic mutations associated with resistance to AZT and 3TC after combination treatment with indinavar'. Int Conf AIDS. 1998, Vol 12, Abstract No. 42197, page 812.					
X Further documents are listed in the continuation of Box C. See patent family annex.						
_	• Special extogories of cited documents: "I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand					
*A" document de to be of part	stining the general state of the art which is not considered tioular relevance	the principle or theory underlying the	invention			
•	ment published on or after the international filing date	"X" document of particular relovance; the considered novel or cannot be considered.	e claimed invention cannot be tred to involve an inventive step			
cited to esta	hich may throw doubts on priority claim(s) or which is blish the publication date of mother citation or other	"Y" document of particular relevance; th	e claimed invention cannot be			
-	on (es specified) Serring to an oral disclosure, use, exhibition or other	considered to involve an inventive combined with one or more other suc being obvious to a person skilled in	h documents, such combination			
	chlished prior to the international filing date but later than date claimed	"&" document member of the same paten	t family			
	completion of the international search	Date of mailing of the international se	arch report			
21 SEPTEMBER 2000		130 672	000			
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231		Authorized officer SHANON FOLEY	ye Burgo			
Facsimile No. (7	03) 305-3230	Telephone No. (703) 898-0196				



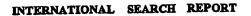
International application No. PCT/US00/17178

C (Continua	tion). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.
K	YOUNG, B. et al. Resistance mutations in protease and reverse transcriptase genes of human immunodeficiency virus type 1 isolates from patients with combination retroviral therapy failure. J. Infectious Diseases. 1998, Vol. 178, pages 1497-1501, see especially page 1498.		34-44
			·
		34	
		·.	

INTERNATIONAL SEARCH REPORT

International application No. PCT/US00/17178

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)				
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:				
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:				
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:				
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).				
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)				
This International Searching Authority found multiple inventions in this international application, as follows:				
Please See Extra Sheet.				
1. X As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.				
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.				
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:				
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:				
Remark on Protest				
No protest accompanied the payment of additional search fees.				



International application No. PCT/US00/17178

B. FIELDS SEARCHED

Blectronic data bases consulted (Name of data base and where practicable terms used):

US PATENTS, IBM TDB, JPO, EPO, DERWENT, MEDLINE, AIDSLINE, BIOSIS, EMBASE search terms: HIV, drug resist, codon, codons, mutat, amprenavir, nelfinavir, ritonavir, saquenavir, indinavir, 90, 73, 77, 10, 20, 88, 77, 63, 46, 10, 82, 54, 24, protease, vector

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be scarched, the appropriate additional search fees must be paid.

Group I, claim(s)1-12, drawn to Diagnostic method involving evaluating patient sample for mutation at codon 88. Group II, claim(s) 13-20, drawn to testing method involving introducing mutation at codon 88 into patient sample. Group III, claim(s) 21 and 79, drawn to method for evaluating viral fitness.

Group III, claims (8) 21 and '9, grawn to memod for evaluating vital indices.

Group IV, claims 22-44,68-70 drawn to Diagnostic method involving evaluating patient sample for mutation at codon

82.

Group V, claim(s)71, 72, 75-78, drawn to testing method involving introducing mutation at codon 82 into patient

sample.

Group VI, claims 45-70, drawn to Diagnostic method involving evaluating patient sample for mutation at codon 90.

Group VII, claim(s)73-75, 78, drawn to testing method involving introducing mutation at codon 90 into patient sample.

The inventions listed as Groups I-VII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Groups (I, IV, VI) and (II, V, VII) require different special technical features, because group (I, IV, VI) involves determination of whether or not a mutation exists at a specific codon in a patient sample, while group (II, V, VII) requires introducing a mutation at the specific codon into a patient sample. (I, II), (IV, V), and (VI, VII) all require different special technical features, because each requires analysis or mutation of a different specific codon.

III does not share the same or corresponding special technical feature of group I, because it does not require the specific codon required in group I.